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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,333	02/10/2004	Michael Moshman	077350.0136	1725

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EXAMINER	
MERCIER, MELISSA S	
ART UNIT	PAPER NUMBER
1615	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/776,333	MOSHMAN ET AL.	
	Examiner	Art Unit	
	Melissa S. Mercier	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5-7-04, 6-24-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on February 2nd, 2007 is acknowledged. The traversal is on the ground(s) that the process as defined in claims 18-19, is directed to defining the product in terms of process it is made and must therefore be rejoined. This is not found persuasive because as discussed in the Election Restriction Requirement dated January 9th, 2007, the product can also be made according to the process disclosed by Ecanow (US Patent 4,963,367). Additionally applicant cites MPEP 821.04(b), stating "if applicant elects a claim directed to a product which is ***subsequently found allowable***, withdrawn process claims which depend from or otherwise require all the limitations of an allowable product claim will be considered for rejoinder".

The examiner acknowledges and thanks applicant for pointing out the error in the cited claims of the Restriction Requirement. Below is the corrected groups and claims contained therein:

I. Claims 1-17 and 20-23, drawn to an aqueous transmucosally delivered controlled release composition and a method for administration, classified in class 424, subclass 449.

II. Claims 18-19, drawn to a method of making an aqueous transmucosally delivered controlled release composition, classified in class 424, subclass 447.

The requirement is still deemed proper and is therefore made FINAL.

Therefore, Claims 1-17 and 20-23 will be examined as part of this office action; claims 18-19 have been withdrawn from consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 and 20-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear to the examiner how the composition can be aqueous when water is an optional component. Clarification is requested.

It is further unclear what a "therapeutically effective" and "an effective amount" are. It is unclear exactly how much is effective and what the desired effect actually is.

Claims 14-15 recites the limitation "antimicrobial agent" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 12 does not further limit the composition to include an antimicrobial agent.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7-8, 16-17, and 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Illum (US Patent 5,629,011).

Illum discloses a composition for nasal administration of polar metabolites of opiod analgesics, including metabolites of morphine; and an absorption-promoting agent, including chitosan (abstract). Chitosan is discloses a being employed to improve the dissolution of poor soluble drugs or for sustained release of drugs by a process of slow erosion from a hydrated compressed matrix (column 3, lines 39-48). Illum discloses the concentration of the cationic polymer is present in the amount of 0.01-50%

w/v (column 4, lines 5-7). Illum discloses the preparation of chitosan micro spheres comprising chitosan dissolved in water with a morphine metabolite incorporated into the micro sphere in which the particles may have variable controlled release characteristics through modifications made to the micro sphere system, for example by controlling the degree of cross-linking or by the incorporation of excipients that alter the diffusion properties of he administered drug (column 6,lines 30-65).

The instant claims differ from the references only in the specific percentage selected for the compositions. However, It would have been deemed prima Facie obvious to one having ordinary skill in the art at the time of the invention to optimize the percentage of active ingredient and the controlled releasing polymer, to prepare a composition containing a therapeutically effective amount of an active agent because the determination of a specific percentage having the optimum therapeutic effect is well within the level of one having ordinary skill in the art, and the artisan would be motivated to determine optimum amounts to get the maximum effect of the active compounds. Therefore, the invention as Whole has been prima face obvious to one of ordinary skill in the art at the time the invention was made.

Applicant is reminded that where the general conditions of the claims are met, burden is shitted to applicant to provide a patentable distinction. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. See In re Aller, 220 F.2d 454 105 USPQ 233,235 (CCPA 1955).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various transmucosal compositions having various amounts of the active agent and chitosan polymers is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. See In re Russell, 439 F.2d 1228 169 USPQ 426(CCPA 1971).

Claims 1-5, 7-12, 16-17, 20-21, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hansen et al. (US Patent 5,955,502).

Hansen discloses the use of a fatty acid ester as bioadhesive substances and methods for administering an active or protective substance to undamaged or damaged skin or mucosa of an animal such as a human by combining the active substance with a bioadhesive fatty acid ester. The mucosa can include oral, aural, nasal, lung, gastrointestinal, vaginal and rectal mucosa (abstract).

The composition of Hansen further comprises chitosan (column 12, lines 59-64), active agents, including morphine (column 11, line 25), antioxidants, including ascorbic acid and derivatives (column 14, lines 64-68), and antimicrobials (column 10, lines 23-24).

Applicants have defined the antioxidants as being used to adjust the pH of the composition (Specification, page 8, lines 3-11), therefore, it is the examiners position that it would have been obvious to a person of ordinary skill in the art to use

methanesulphonic acid, citric acid, sodium citrate, or sodium ascorbate to adjust the pH of the composition. It is generally considered to be prime facie obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for combining them flows from their having been used individually in the prior art, and from them being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the combination of conventional components of pH adjusting components and antimicrobial agents. It therefore follows that the instant claims define prime facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

The instant claims differ from the references only in the specific percentage selected for the compositions. However, It would have been deemed prima Facie obvious to one having ordinary skill in the art at the time of the invention to optimize the percentage of active ingredient and the controlled releasing polymer, to prepare a composition containing a therapeutically effective amount of an active agent because the determination of a specific percentage having the optimum therapeutic effect is well within the level of one having ordinary skill in the art, and the artisan would be motivated to determine optimum amounts to get the maximum effect of the active compounds. Therefore, the invention as Whole has been prima face obvious to one of ordinary skill in the art at the time the invention was made.

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various

transmucosal compositions having various amounts of the active agent and chitosan polymers is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. See In re Russell, 439 F.2d 1228 169 USPQ 426(CCPA 1971).

Claims 1-5, 7-17, and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dellamary et al. (US Patent 6,433,040).

Dellamary discloses methods, systems, and compositions comprising relatively stable dispersions of perforated microstructures in a suspension medium that are preferably administered vial liquid doe instillation, both for topical delivery to the lung and for delivery via the lung to the systemic circulation (column 1, lines 16-25). The composition may also be administered topically, subcutaneously, intramuscularly, intraperitoneally, nasally, vaginally, rectally, orally, or ocularly (column 9, lines 62-65). The dispersion comprising a structural matrix defining the perforated microstructure and may comprising polysaccharides such as chitosan (column 18, lines 2-7). Dellamary discloses those skilled in the art will appreciate that by selecting the appropriate polymers, the delivery profile of the respiratory dispersion may be tailored to optimize the effectiveness of the bioactive agent (column 18, lines 8-11). Antioxidants may also be incorporated into the dispersions, including sodium citrate and sodium ascorbate (column 18, lines 33-37). Morphine is discloses as a medicant or bioactive agent suitable for use in the dispersion (column 19, lines 45-47). The suspensions mediums

additionally comprise fluorochemicals, with are also bacteriostatic thereby decreasing the potential for microbial growth in compatible preparations (column 5, line 66 through column 6. line 11). The examiner is interpreting the fluorochemicals to be antimicrobial agents.

Dellamary further discloses the precise amount of bioactive agent incorporated into the stabilized dispersions is dependent upon the agent of choice, the volume of suspension media required to effectively distribute the drug, the required dose and the form of the drug actually used for incorporation. Those skilled in the art will appreciate that; such determination may be made by using well-known pharmacological techniques in combination with the teachings of the Dellamary disclosure (column 19, lines 13-21).

Applicants have defined the antioxidants as being used to adjust the pH of the composition (Specification, page 8, lines 3-11), therefore, it is the examiners position that it would have been obvious to a person of ordinary skill in the art to use methanesulphonic acid, citric acid, sodium citrate, or sodium ascorbate to adjust the pH of the composition. It is generally considered to be prime facie obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for combining them flows from their having been used individually in the prior art, and from them being recognized in the prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the combination of conventional components of pH adjusting components and antimicrobial agents. It

therefore follows that the instant claims define prime facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

The instant claims differ from the references only in the specific percentage selected for the compositions. However, It would have been deemed prima Facie obvious to one having ordinary skill in the art at the time of the invention to optimize the percentage of active ingredient and the controlled releasing polymer, to prepare a composition containing a therapeutically effective amount of an active agent because the determination of a specific percentage having the optimum therapeutic effect is well within the level of one having ordinary skill in the art, and the artisan would be motivated to determine optimum amounts to get the maximum effect of the active compounds. Therefore, the invention as Whole has been prima face obvious to one of ordinary skill in the art at the time the invention was made.

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various transmucosal compositions having various amounts of the active agent and chitosan polymers is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. See In re Russell, 439 F.2d 1228 169 USPQ 426(CCPA 1971).

Claims 1-17 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Illum et al. (US Patent 6,387,917).

Illum discloses a methane sulphonate salt of morphine and compositions thereof having medicinal uses, particularly for the treatment of pain and adapted for nasal delivery (abstract). The preferred composition comprises aqueous solutions in which the methane sulphonate salt is combined with chitosan to provide an increased absorption of the drug (column 2, lines 61-68). The morphine methane sulphonate liquid formulation will comprise 0.1mg/mL to about 600mg/mL (column 4, lines 20-24). The formulation may also be incorporate into formulations suitable for oral, buccal, rectal, or vaginal administration (column 4, lines 39-42). Illum's Examples 2-3 discloses a solution for intranasal administration comprising morphine base (monohydrate) and chitosan (column 5, line 33 through column 6, line 21).

Illum further discloses the formulation can also contain other ingredients such as buffer systems, pH modifiers, anti-oxidants, stabilizing agents, anti-microbial agents, chelating agents, viscosity-enhancing agents, or other agents generally used in pharmaceutical formulations (column 4, lines 25-29). Applicants have defined the antioxidants as being used to adjust the pH of the composition (Specification, page 8, lines 3-11), therefore, it is the examiners position that it would have been obvious to a person of ordinary skill in the art to use methanesulphonic acid, citric acid, sodium citrate, or sodium ascorbate to adjust the pH of the composition. It is generally considered to be prime facie obvious to combine compounds each of which is taught by the prior art to be useful for the same purpose in order to form a composition that is to be used for an identical purpose. The motivation for combining them flows from their having been used individually in the prior art, and from them being recognized in the

prior art as useful for the same purpose. As shown by the recited teachings, instant claims are no more than the combination of conventional components of pH adjusting components and antimicrobial agents. It therefore follows that the instant claims define prime facie obvious subject matter. Cf. In re Kerhoven, 626 F.2d 848, 205 USPQ 1069 (CCPA 1980).

The instant claims differ from the references only in the specific percentage selected for the compositions. However, It would have been deemed prima Facie obvious to one having ordinary skill in the art at the time of the invention to optimize the percentage of active ingredient and the controlled releasing polymer, to prepare a composition containing a therapeutically effective amount of an active agent because the determination of a specific percentage having the optimum therapeutic effect is well within the level of one having ordinary skill in the art, and the artisan would be motivated to determine optimum amounts to get the maximum effect of the active compounds. Therefore, the invention as Whole has been prima face obvious to one of ordinary skill in the art at the time the invention was made.

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various transmucosal compositions having various amounts of the active agent and chitosan polymers is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. See In re Russell, 439 F.2d 1228 169 USPQ 426(CCPA 1971).

Conclusion

No claims are allowable. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa S. Mercier whose telephone number is (571) 272-9039. The examiner can normally be reached on 7:30am-4pm Mon through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MSMercier

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